Antidepressant-like Effect and the Mechanism of Action of Lippia Citriodora Ethanolic Extract and Emulsion, and Verbascoside

著者（英）	Mouad SABTI
内容記述	この博士論文は内容の要約のみの公開（または一部非公開）になっています
year	2019
その他のタイトル	ベルベナ抽出物由来活性成分の抗うつ様作用評価およびエマルジョンによる活性成分の安定化
学位授与大学	筑波大学 (University of Tsukuba)
学位授与年度	2019
報告番号	12102甲第9334号
URL	http://hdl.handle.net/2241/00160410

Antidepressant-like Effect and the Mechanism of Action of *Lippia Citriodora* Ethanolic Extract and Emulsion, and Verbascoside

August 2019

Mouad SABTI

Antidepressant-like Effect and the Mechanism of Action of *Lippia Citriodora* Ethanolic Extract and Emulsion, and Verbascoside

A Dissertation Submitted to
The School of the Integrative and Global Majors,
The University of Tsukuba
in Partial Fulfillment of the Requirements
for the Degree of Doctor of Philosophy in Drug discovery
(Doctoral Program in Life Science Innovation)

Mouad SABTI

Summary

Lippia citriodora (Lam.), commonly called lemon verbena or "*Louisa*" (Arabic), is an aromatic and medicinal plant rich in terpens and polyphenols used in folk medicine to cure illnesses such as gastrointestinal disorders, fever and headaches and also for its sedative and relaxant properties. The chemical analysis of verbena extract has been shown to contain different compounds, with verbascoside (Vs) as major compound, a phenypropanoid glycoside. A previous study demonstrated, according to traditional information, the relaxant and hypnotic properties of *L. citriodora* and Vs *in vivo* using rotarod test. However, the antidepressant-like effect of the verbena and Vs were not studied *in vivo* and *in vitro* and their molecular mechanisms are still to be elucidated. In this work, the antidepressant-like effect of verbena ethanolic extract (VEE) and Vs was evaluated using on a tail suspension test (TST) and confirmed the results *in vitro* using human neurotypic SH-SY5Y cells. VEE and Vs regulated expression of genes implicated in production of cAMP (such as *Adenylate cyclase*) and increased intracellular calcium levels, including *Inositol 1,4,5-trisphosphate receptor type 2*.

TST was conducted on mice treated orally with VEE (100 mg /kg), Vs (2.5 and 5 mg/kg), Bupropion (20 mg /kg) and Milli-Q water. VEE-treated mice showed an increase of immobility time compared to control groups, indicating an induction of relaxation. This effect was found to be induced by regulation of genes playing key roles in calcium homeostasis (calcium channels), cAMP production and energy metabolism. On the other hand, Vs showed antidepressant-like effect and was confirmed by serotonin, noradrenalin, dopamine and BDNF expressions. Finally, VEE and Vs enhanced SH-SY5Y cells viability, mitochondrial activity and calcium uptake *in vitro*. The obtained results showed induction of relaxation and antidepressant-like effects VEE and Vs, respectively, through modulation of cAMP and calcium.

Furthermore, studying the ways of industrialization of VEE and Vs in food area is of a great importance. Production of emulsion based on VEE to enhance storage time and deliverance of Vs was carried out. Formulation of VEE based emulsion including lecithin and oleic acid was found to be stable after storage for more than 2 weeks.

This VEE-emulsion was found to exert antidepressant-like effect *in vivo* by reducing the immobility time of mice in TST. Also it enhanced different depression markers and genes expressions that were affected by VEE solution. Understanding the molecular mechanism by which Vs and VEE, in solution or emulsion, induce the antidepressant-like effect is essential.